Complete Summary

GUIDELINE TITLE

Guidelines for the management of uterine fibroids.

BIBLIOGRAPHIC SOURCE(S)

New Zealand Guidelines Group. Guidelines for the management of uterine fibroids. Wellington (NZ): New Zealand Guidelines Group (NZGG); 1999 Aug. 120 p. [182 references]

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Uterine fibroids (myomas or leiomyomas)

GUIDELINE CATEGORY

Diagnosis
Management
Treatment

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Obstetrics and Gynecology

INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel

Nurses
Patients
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To provide evidence-based recommendations to assist decision making for the management of women who have uterine fibroids.

TARGET POPULATION

Women, including pregnant women, with or suspected of having uterine fibroids

INTERVENTIONS AND PRACTICES CONSIDERED

Assessment

1. Observation and/or referral to a specialist in asymptomatic women
2. Transvaginal ultrasound; transabdominal ultrasound
3. Transvaginal sonohysterography
4. Hysteroscopy
5. Magnetic resonance imaging in select cases

NOTE: Computerised tomography (CT) scanning, and magnetic resonance imaging (MRI) as an initial diagnostic test, were considered.

Medical Management

1. Combined oral contraceptives
2. Gestrinone
3. Gonadotrophin-releasing hormone analogues alone and followed by combined 'addback' therapy (oestrogen plus progestin)
4. Hormone replacement therapy adjustments in women who bleed while on hormone replacement therapy and who are known to have fibroids

NOTE: Progestogens, hormone replacement therapy, transdermal oestrogen formulations, and Danazol were considered but are not recommended.

NOTE: Antiprogestins, such as mifepristone (RU486, which is not currently available in New Zealand); non-steroidal anti-inflammatory drugs (NSAIDs); and progestogen-releasing intrauterine systems, such as levonorgestrel intrauterine system were considered.

Pre-operative management

1. Gonadotrophin-releasing hormone analogues in select cases

Surgical Management

1. Hysteroscopic ablation or resection
2. Myomectomy
3. Hysterectomy
4. Embolisation of uterine fibroids

NOTE: Additional surgical interventions that were considered but not recommended based on insufficient evidence include: laser-induced interstitial thermotherapy, myolysis or cryomyolysis; routine use of vasopressin in reducing operative blood loss; and routine use of adhesion barriers.

Management during Pregnancy

1. Referral to a specialist

MAJOR OUTCOMES CONSIDERED

The following outcome measures were used in the development of the diagnostics evidence tables:

- Sensitivity and specificity
- Prevalence (pretest probability)
- Positive and negative likelihood ratios

The following outcome measures were considered when deciding on medical treatment options for uterine fibroids:

- Uterine and fibroid volume/fibroid regrowth
- Uterine/myoma size
- Menstrual blood loss
- Pituitary-ovarian function
- Bone metabolism/bone mineral density
- Estradiol, gonadotropin and lipid levels
- Haemoglobin/haematocrit
- Adverse effects

The following outcomes measures were considered when deciding on pre-operative medical treatment options for uterine fibroids:

- Uterine and fibroid volume/fibroid regrowth
- Fibroid/Myoma recurrence
- Change in symptoms
- Haemoglobin/haematocrit
- Intraoperative blood pressure/changes in pulse
- Operative blood loss/need for blood transfusion/transfusion rate
- Postoperative morbidity/pain
- Length of hospital stay
- Menstrual status including bleeding and menstrual pain
- Side effects/complications of the surgery and total operating times
- Type of abdominal incision
- Quality of life

The following outcome measures were considered when deciding on surgical options for uterine fibroids:

- Incidence, severity, extent and area of uterine adhesions at follow-up laparoscopy/adhesion score
- Haemoglobin/Hct
- Intraoperative blood pressure/changes in pulse
- Blood loss/need for blood transfusion
- Postoperative morbidity/pain
- Length of hospital stay
- Menstrual status including bleeding and menstrual pain
- Side effects/complications of the surgery and total operating times

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases
Searches of Unpublished Data

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

For each question and topic, evidence was sought from original scientific publications, systematic reviews or meta-analyses. Comparative studies and randomised controlled trials (RCTs) were sought for evidence for diagnostic tests (see search strategy described below). Electronic searches were undertaken using MEDLINE (1966-1999), EMBASE and smaller databases such as Current Contents, Biological Abstracts, Social Sciences Index, PsychLIT and CINAHL (Cumulative Index to Nursing and Allied Health). Attempts were also made to identify and include unpublished work and conference abstracts. The database of the Cochrane Menstrual Disorders and Sub-Fertility Group (which included the efforts of handsearching) was made available to the Working Party. For some trials extra data were made available by the researchers. The full text of all publications was sought.

The literature search for diagnostic studies used the key words leiomyoma, fibromyoma, fibroma, fibroid, myoma, adenomyoma, hysteroscopy, hystero, hysterosonography, ultrasound, ultrasonography, transvaginal sonography, magnetic resonance imaging, tomography (x-ray computed) and was limited to the English language. The search and subsequent reference trails generated by the articles revealed over 200 papers. As a means of culling papers, studies were excluded if they had less than 50 women in them or were published before 1989.

Therapeutic studies were identified using the key words fibroids, myoma, leiomyoma, adenomyoma. All identified RCTs were sought and in some cases systematic reviews were available.

NUMBER OF SOURCE DOCUMENTS

Over 200

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

The Working Party agreed to rank the evidence using the Revised SIGN Grading System (Scottish Intercollegiate Guidelines Network [SIGN] 2000) as follows:

Levels of Evidence:

1+ +

High quality meta-analyses, systematic reviews of randomized controlled trials (RCTs), or RCTs with a very low risk of bias

1+

Well-conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias

1-

Meta analyses, systematic reviews, or RCTs with a high risk of bias

2+ +

High quality systematic reviews, or RCTs with a high risk of bias

2+ +

Well-conducted case control or cohort studies with a low risk of confounding or bias and a high probability that the relationship is causal

2+

Well-conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal

2-

Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is causal

3

Non-analytic studies, such as case reports or case series

4

Expert opinion

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

The evidence from identified literature was summarised into evidence tables (see section 3 of the original guideline). A detailed explanation of the methods used in the development of the evidence tables is provided in Appendix 5.4 of the original guideline.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

A multidisciplinary working party with representation from both professional and consumer groups undertook the preparation of this guideline in association with the New Zealand Guidelines Group. Their first meeting was in March 1999 and the concept of guideline development was presented to the group. The next meeting was held in May 1999. This was very much a working meeting with members discussing some of the more difficult issues. The final meeting was held in September 1999. Not all members were able to attend all meetings but were circulated with drafts and minutes of the meetings.

Various members undertook to write sections of the Guideline. Dr C Farquhar collated these sections and produced a draft Guideline that was circulated in August 1999 to interested groups and individuals. Comments were invited and four weeks given for response to be returned. A final draft was circulated to the working party members in September 1999.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Grading the Recommendations

Grade A*

- At least one meta-analysis, systematic review or RCT graded as 1++, and directly applicable to the target population; or
- A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results

Grade B

- A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; or
- Extrapolated evidence from studies rated as 1++ or 1+

Grade C

- A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; or
- Extrapolated evidence from studies rated as 2++

Grade D

- Evidence level 3 or 4; or
- Extrapolated evidence from studies rated as 2+

* The present grading system differs from the Scottish Intercollegiate Guidelines Network (SIGN) grading system in that comparative cross-sectional studies that met the criteria for quality diagnostics were given a rating of "Grade A."

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

A draft guideline was circulated to interested groups and individuals. Comments were invited and four weeks given for response to be returned. (Groups and individuals who made comments on the draft were acknowledged by name in the guideline document.) A final draft was circulated to the working party members.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Note: Recommendation grades (A-D) and associated levels of evidence are defined at the end of the Major Recommendations field.

I. Assessment

- Asymptomatic women with fibroids in whom the uterine size is less than 16 weeks (and where other causes of pelvic mass have been excluded) do not need further investigations but should be advised to seek medical advice if symptoms occur [D].
- Asymptomatic women with fibroids >16/40 should have specialist referral to discuss options including observation [D].

- Although there is no evidence that asymptomatic women with a fibroid uterus greater than 20 weeks will have future health problems, hysterectomy or myomectomy is an option [D].
- The low incidence of leiomyosarcoma discovered incidentally in asymptomatic women with uterine fibroids does not support the operative management of fibroids as prevention of leiomyosarcoma [D].
- Transvaginal ultrasound of the endometrium is accurate in excluding endometrial hyperplasia but is often unable to distinguish submucosal fibroids and polyps [A].
- Transabdominal ultrasound may be required for uteri greater than 12 weeks' size as these will be beyond the reach of the transvaginal ultrasound [D].
- Transvaginal ultrasound and transvaginal sonohysterogram are both more accurate in diagnosing the location of fibroids than hysteroscopy [A].
- Transvaginal sonohysterography should be considered prior to hysteroscopy in women in whom intrauterine pathology such as submucous fibroids and polyps are suspected as diagnostic hysteroscopy can be avoided in up to 40% of women [A].
- When recommending hysteroscopy the following points should be considered:
    - Normal saline should be used as it offers advantages (shorter and less discomfort) over carbon dioxide instillation [A].
    - Local anaesthetic should be offered as either a paracervical block, uterosacral block or uterine instillation [A].
- There is insufficient evidence to recommend computerised tomography scanning in the assessment of fibroids [D].
- There is insufficient evidence to recommend magnetic resonance imaging (MRI) scanning as an initial diagnostic test for uterine pathology [D].
- MRI should be considered for women in whom the location or nature of the fibroids remains uncertain after transvaginal ultrasound and transvaginal sonohysterography or if they wish to avoid the possible discomforts of a transvaginal sonohysterography [D].

II. Medical Management

- Progestogens should not be recommended in the treatment of uterine fibroids as there is insufficient evidence of benefit [D].
- Oral contraceptives are not effective in shrinking uterine size but may reduce menstrual blood loss with a resultant improvement in haematocrit [C].
- RU486 is effective in reducing uterine fibroid size without causing a reduction in bone mineral density [D].
- Danazol should not be recommended as initial treatment for fibroids as it is not as effective as gonadotrophin-releasing hormone analogues and has androgenic side effects which limit its use [C].
- Gestrinone is effective in reducing uterine and fibroid size but its androgenic side effects may limit its use [A].
- Non-steroidal anti-inflammatory drugs (NSAIDs) are not effective as a treatment for women with fibroids in reducing heavy menstrual bleeding [B].

- Gonadotrophin-releasing hormone analogue treatment effectively reduces uterine and fibroid size but unpleasant side effects and a reduction in bone mineral density limit its sole use to 6 months [A].
- Gonadotrophin-releasing hormone analogue treatment for 3 months followed by combined â ˜addback´ therapy (oestrogen plus progestin) results in fibroid shrinkage and is an alternative for women who have contraindications to surgery or who do not wish to undergo surgery. Once therapy stops the fibroids will return to pretherapy size [B].
- There is insufficient evidence to recommend progestogen-releasing intrauterine systems to reduce uterine fibroid size [C].
- Hormone replacement therapy (HRT) should not be used to treat fibroids as it is not effective in reducing uterine fibroid size [A].
- Women who bleed while on continuous combined HRT and who are known to have fibroids should have adjustments made to their HRT by either decreasing the oestrogen dose or increasing the progesterone dose [D].
- Transdermal oestrogen formulations should not be given to women with fibroids [A].

III. Pre-Operative Management

- Administration of Gonadotrophin-releasing hormone analogues for 2 to 4 months prior to surgery for uterine fibroids is recommended for women with a large uterus (>18 weeks size) or pre-operative anaemia [B].

IV. Surgical Management

- Women who are diagnosed with submucous uterine fibroids and heavy or abnormal menstrual bleeding should be offered hysteroscopic ablation or resection as an alternative to hysterectomy [C].
- Women with subserous and intramural fibroids associated with symptoms such as heavy menstrual bleeding and pressure symptoms should be offered a myomectomy as an alternative to hysterectomy [D].
- The decision whether a hysterectomy or myomectomy is undertaken is dependent on: the woman´s preference, the age of the woman, the desire to retain reproductive potential and the position and number of the fibroids [D].
- Laparoscopic myomectomy should not be undertaken in women who wish to conceive because of case reports suggesting increased risk of uterine rupture [D].
- There is insufficient evidence to recommend the routine use of adhesion barriers [B].
- There is insufficient evidence to recommend the routine use of vasopressin in reducing operative blood loss [C].
- There is insufficient evidence to support the introduction of laser-induced interstitial thermotherapy, myolysis or cryomyolysis technique [D].
- The low incidence of leiomyosarcoma discovered incidentally in asymptomatic women with uterine fibroids does not support the operative management of fibroids as prevention of leiomyosarcoma [D]
- Embolisation of uterine fibroids may be an effective alternative to myomectomy or hysterectomy but randomised controlled trials (RCTs) are awaited [D].

V. Management during Pregnancy

- Women who have fibroids detected during pregnancy should be referred to a specialist for a consult but do not require additional surveillance unless symptoms arise during the pregnancy [D].

Definitions:

Recommendations Grades

Grade A*

- At least one meta-analysis, systematic review or randomized controlled trial (RCT) graded as 1++, and directly applicable to the target population; or
- A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results

Grade B

- A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; or
- Extrapolated evidence from studies rated as 1++ or 1+

Grade C

- A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; or
- Extrapolated evidence from studies rated as 2++

Grade D

- Evidence level 3 or 4; or
- Extrapolated evidence from studies rated as 2+

Levels of Evidence

1+ +

High quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias

1+

Well-conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias

1-

Meta analyses, systematic reviews, or RCTs with a high risk of bias

2+ +

High quality systematic reviews, or RCTs with a high risk of bias

2+ +

Well-conducted case control or cohort studies with a low risk of confounding or bias and a high probability that the relationship is causal

2+

Well-conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal

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Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is causal

3

Non-analytic studies, such as case reports or case series

4

Expert opinion

CLINICAL ALGORITHM(S)

The original guideline document contains an algorithm for the management of the premenopausal woman with suspected uterine fibroids.

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

In the therapeutics section, systematic reviews or randomized controlled trials (RCTs) were sought wherever possible and recommendations were based on such evidence. Where evidence was weaker or lacking, recommendations were based on the best available evidence from either case control, cohort studies or case series or expert opinion. For diagnostic testing comparative studies were sought.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate management of uterine fibroids may lead to decreased hysterectomy rates, increased use of medical therapy, and appropriate use of diagnostic tests.

Resolution of symptoms of heavy menstrual blood loss and abnormal uterine bleeding, and relief of pressure symptoms may result if fibroids are removed. Data supporting the benefits of specific interventions and practices may be found in the guideline document.

POTENTIAL HARMS

Potential harms associated with assessment of fibroids:

- Transvaginal sonography will not see large pedunculated fibroids nor large fibroid uteria and transabdominal ultrasound may be necessary.
- Transvaginal sonography may miss polyps and submucosal fibroids.
- Transvaginal sonohysterography may miss fibroids <0.5 cm. Some discomfort from the distension may be experienced. Infective complications are rare.
- Hysteroscopy is not as good as transvaginal sonography or transvaginal sonohysterography for hyperplasia.
- Computed tomography is not as specific as ultrasound in differentiating uterine masses from ovarian masses or surrounding bowel.

Side effects associated with pharmacotherapy:

- Oral contraceptives are associated with nausea, headache, and breast tenderness.
- Gestrinone is associated with androgenic side effects, such as such as acne, hirsutism, and weight gain.
- Gonadotrophin-releasing hormone analogues. There are significant disadvantages to the use of gonadotrophin-releasing hormone analogues as a sole treatment for uterine fibroids. The duration of treatment with these agents is limited to six months because of the rapid bone demineralisation associated with oestrogen withdrawal. Furthermore, the occurrence of subjective side effects associated with the hypo-oestrogenic state, particularly hot flushes and vaginal dryness, are unpleasant and can reduce quality of life. After GnRH analogue therapy is stopped, there is regrowth of both fibroids and uterus to almost pre-treatment size and a recurrence of symptoms in most women. For this reason, the use of GnRH analogues as a sole treatment for uterine fibroids is disappointing.
- Hormone replacement therapy increases the frequency of abnormal bleeding in pre- and post-menopausal women with fibroids. However, the extent to which hormone replacement therapy increases the frequency of abnormal bleeding is not known, which is due, in part, to dissimilar study definitions of abnormal bleeding and different treatment regimens.

Potential harms associated with surgical management:

- Gonadotrophin-releasing hormone analogue pretreatment prior to either hysterectomy or myomectomy may be associated with uncomfortable adverse events such as headaches, hot flushes, and vaginal symptoms. There is some evidence to suggest that women with gonadotrophin-releasing hormone analogue pretreatment may be more likely to have their fibroids recur (an average of 4 times the odds), presumably because small fibroids are not seen at the time of surgery.

- Hysteroscopy. Operative complications of hysteroscopic fibroid resection may include incomplete resection, fluid absorption > 2000ml, cervical tear, blood transfusion and uterine perforation.
- Myomectomy. Scar rupture in late pregnancy may rarely occur (0.5% of cases) following myomectomy. Uterine rupture during pregnancy following laparoscopic myomectomy has been reported.
- Myolisis. Uterine rupture at the site during pregnancy has been reported, and, as a result, the technique is not widely used.
- Hysterectomy. Although hysterectomy is curative for uterine fibroids, it has the drawback of removing future fertility.
- Embolisation of fibroids (uterine artery embolisation). Complications following uterine artery embolisation were reported in 4 to 25% of cases and included fibroid expulsion through the cervix (requiring hysterectomy), fibroid necrosis, severe pain, and fever requiring hospital admission. Discomfort may occur in the first weeks following the procedure.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

The guideline does not provide recommendations for the investigation of undiagnosed abdominal masses.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

The following areas need to be considered in the implementation of these guidelines.

- Training for transvaginal sonohysterography
- Linkage to other guidelines, particularly the guidelines for management of heavy menstrual bleeding
- Increased access to gonadotropin-releasing hormone analogue/RU486 as preoperative and medical therapy; and to transvaginal sonography/transvaginal sonohysterography for diagnosis

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

New Zealand Guidelines Group. Guidelines for the management of uterine fibroids. Wellington (NZ): New Zealand Guidelines Group (NZGG); 1999 Aug. 120 p. [182 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1999 Aug

GUIDELINE DEVELOPER(S)

New Zealand Guidelines Group - Private Nonprofit Organization

SOURCE(S) OF FUNDING

The development of the guideline was funded in part by a grant from the New Zealand National Health Committee. This covered the cost of the meetings, identification of the evidence and secretarial costs of preparing the manuscript.

GUIDELINE COMMITTEE

Guideline Development Working Party

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Members of Guideline Development Group: Cindy Farquhar; Bruce Arroll; Alec Ekeroma; Gary Fentiman; Anne Lethaby; Linda Rademaker; Helen Roberts; Lynn Sadler; Judi Strid.

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

At the first meeting, all members of the Guideline Development Working Party agreed to declare any interests or connections with relevant pharmaceutical companies or other organizations. No member had any paid consultancy or any other conflict of interest with any pharmaceutical company currently involved with therapeutic products for fibroids.

GUIDELINE STATUS

This is the current release of the guideline.

An update is not in progress at this time.

GUIDELINE AVAILABILITY

Electronic copies: Available from the New Zealand Guidelines Group Web site.

Print copies: Available from the New Zealand Guidelines Group Inc., Level 30, Grand Plimmer Tower, 2-6 Gilmer Terrace, PO Box 10-665, Wellington, New Zealand; Tel: 64 4 471 4188; Fax: 64 4 471 4185; e-mail: info@nzgg.org.nz.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on October 17, 2000. The information was verified by the guideline developer on November 21, 2000.

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